

CLAIMS

1. Method of preparation of a population of circulating cells capable of regenerating hematopoiesis in vivo comprising:

- a) administering to a donor a composition comprising growth hormone or one of its derivatives or any factor inducing growth hormone release in an amount sufficient to increase in said donor the number of circulating cells capable of regenerating hematopoiesis in vivo.
- b) isolating a population of circulating cells capable of regenerating hematopoiesis in vivo from the peripheral blood of said donor.
- c) re-infusing, grafting or transplanting said isolated population into the same individual or into different individuals.

2. Method of preparation of a population of circulating cells capable of regenerating hematopoiesis in vivo comprising:

- a) administering to a donor a composition comprising growth hormone or one of its derivatives or any factor inducing growth hormone release, simultaneously or separately with a composition comprising G-CSF, in an amount sufficient to increase in said donor the number of circulating cells capable of regenerating hematopoiesis in vivo.
- b) isolating a population of circulating cells capable of regenerating hematopoiesis in vivo from the peripheral blood of said donor.

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3. Method of preparation of a population of circulating cells capable of regenerating hematopoiesis in vivo comprising:

a) administering to a donor, over a period of up to 20 days, a composition comprising growth hormone or one of its derivatives or any factor inducing growth hormone release in an amount sufficient to increase in said donor the number of circulating cells capable of regenerating hematopoiesis in vivo.

b) isolating a population of circulating cells capable of regenerating hematopoiesis in vivo from the peripheral blood of said donor.

4. Method according to any one of claims 1 to 3 wherein the circulating cells capable of regenerating hematopoiesis in vivo are CD34<sup>+</sup> cells.

5. Method according to claim 4 wherein the increased number of CD34<sup>+</sup> cells is more than 10, 25, 34 or 80 CD34<sup>+</sup> cells per microliter of donor peripheral blood.

6. Method according to claim 4 wherein the increased number of CD34<sup>+</sup> cells is at least  $2 \times 10^6$ ,  $4 \times 10^6$ ,  $5 \times 10^6$ ,  $6 \times 10^6$ ,  $8 \times 10^6$ ,  $15 \times 10^6$  CD34<sup>+</sup> cells per kilogram of donor body weight.

7. Method according to any one of claims 1 to 3 wherein the increased number of circulating cells capable of regenerating hematopoiesis in vivo corresponds to around or more than 500 CFU-GM per milliliter of donor peripheral blood.

8. Method according to any one of claims 1 to 3 wherein the increased number of circulating cells capable of regenerating hematopoiesis in vivo corresponds to an increased level of CFU-C, CFU-Meg or BFU-E in donor peripheral blood.

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9. Method according to any one of claims 1 to 3 wherein the increased number of circulating cells capable of regenerating hematopoiesis in vivo substantially corresponds to a white blood cell count of around or more than 1000 cells per microliter of donor peripheral blood.

10. Method according to any one of claims 1 to 3 wherein the increased number of circulating cells capable of regenerating hematopoiesis in vivo corresponds to around or more than  $1 \times 10^5$  GM-CFC per kilogram of donor or recipient body weight.

11. Method according to any one of claims 1 to 3 wherein the circulating cells capable of regenerating hematopoiesis in vivo are CD34<sup>+</sup>/CD33<sup>-</sup> cells and/or CD34<sup>+</sup>/CD38<sup>-</sup> cells and/or CD34<sup>+</sup>/Thy-I cells and/or CD34<sup>+</sup>/Thy-I/CD38<sup>-</sup> cells and/or CD33<sup>+</sup> cells and/or bone-marrow stem cells and/or progenitor cells and/or long-term culture initiating cells (LTC-IC) and/or cells that fulfill self renewal potential and/or cells that fulfill pluripotential characteristics and/or cells that initiate long term bone marrow culture and/or cells that can generate multiple cell lineages.

12. Method according to any one of claims 1 to 3 wherein the target number of circulating cells capable of regenerating hematopoiesis in vivo is at least  $2 \times 10^4$  LTC-IC per kg of donor or recipient body, around or more than  $2 \times 10^6$  CD34<sup>+</sup> cells per kilogram of donor or recipient body weight, around or more than  $4 \times 10^6$  CD34<sup>+</sup> cells per kilogram of donor or recipient body weight or around or more than  $8 \times 10^6$  CD34<sup>+</sup> cells per kilogram of donor or recipient body weight.

13. Method according to any one of claims 1 to 3 wherein the volume of blood processed in step (b) is comprised in a range of about 30 to about 900 milliliters.

14. Method according to any one of claims 1 to 3 wherein the composition comprises one or several further compounds chosen among the following groups of compounds: hematopoietic growth factors, cytokines, chemokines, monoclonal antibodies.

15. Method according to claim 1 or 3 wherein the composition is administered simultaneously or separately with one or more further compositions comprising one or several compounds chosen among the following groups of compounds: hematopoietic growth factors, cytokines, chemokines, monoclonal antibodies.

16. Method according to claim 14 or 15 wherein the cytokine group comprises IL-1, IL-3, G-CSF, GM-CSF or SCF; the chemokine group comprises MIP-1 $\alpha$  or thrombopoietin (TPO); the monoclonal antibody group comprises anti-VLA-4 antibodies.

17. Method according to claim 14 or 15 wherein the further compound or composition comprises G-CSF.

18. Method according to any one of claims 1 to 3 wherein growth-hormone or one of its derivatives or any factor inducing growth hormone release is administered in an amount comprised between 20 to 50  $\mu$ g/kg of donor body weight, in an amount comprised between 30 to 40  $\mu$ g/kg of donor body weight or in an amount of 33  $\mu$ g per kilogram of donor body weight.

19. Method according to claim 17 wherein the G-CSF is administered in an amount comprised between 3 to 15  $\mu$ g/kg of donor body weight, in an amount comprised between 4 to 12  $\mu$ g/kg of donor body weight or in an amount of around 5 or 10  $\mu$ g per kilogram of donor body weight.

20. Method according to claim 2 wherein the administration of Growth Hormone is made three times a day and the administration of G-CSF is made daily.

21. Method according to any one of claims 1 to 3 wherein the administration of said composition is made by parenteral, subcutaneous, intravenous, intramuscular, intraperitoneal, transdermal or buccal routes.

22. Method according to any one of claims 1 to 3 wherein the administration of said composition is daily or three times a day.

23. Method according to claim 1 or 2 wherein the administration of said composition is made over a period of 5 days or over a period of 10 days.

24. Method according to any one of claims 1 to 3 wherein the administration begins around 7 days after the beginning of a chemotherapeutic treatment or around 2 days after the end of a chemotherapeutic treatment.

25. Method according to any one of claims 1 to 3 wherein the growth hormone is recombinant growth hormone.

26. Method according to any one of claims 1 to 3 wherein the growth hormone is human growth hormone.

27. Method for the enhancement of hematopoiesis reconstitution in a human being comprising the steps of :

- a) administering to a donor a composition comprising growth hormone or one of its derivatives or any factor inducing growth hormone release in an amount sufficient to increase in said donor the number of circulating cells capable of regenerating hematopoiesis in vivo.

b) isolating a population of circulating cells capable of regenerating hematopoiesis in vivo from the peripheral blood of said donor.

c) transplanting the cells recovered in step (b) to an individual, and

d) administering to this individual growth hormone or one of its derivatives or any factor inducing growth hormone release in an amount sufficient to accelerate hematopoietic recovery.

28. Method according to claim 27 wherein administration in steps a) and d) further encompasses G-CSF.

29. Use of human growth hormone or one of its derivatives or any factor inducing human growth hormone release to prepare a medicament which increases, in a donor, the number of circulating cells capable of regenerating hematopoiesis in vivo, said cells being used to treat by re-infusion, transplantation or engraftment a recipient in need of such cells.

30. Use of human growth hormone or one of its derivatives or any factor inducing human growth hormone release to prepare a medicament to increase in a donor the number of circulating cells capable of regenerating hematopoiesis in vivo available for leukapheresis and re-infusion, transplantation or engraftment in a recipient in need of such cells.

31. Use of human growth hormone or one of its derivatives or any factor inducing human growth hormone release to prepare a medicament, administered separately or simultaneously with G-CSF, to increase the number of circulating cells capable of regenerating hematopoiesis in vivo in a human being.

32. Use of human growth hormone or one of its derivatives or any factor inducing human growth hormone

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release to prepare a medicament to increase over a period of up to 20 days the number of circulating cells capable of regenerating hematopoiesis in vivo in a human being.

33. Use according to any one of claims 29 to 32 wherein the medicament comprises one or several further compound(s) chosen among the following groups of compounds: hematopoietic growth factors, cytokines, chemokines, monoclonal antibodies.

34. Use according to any one of claim 29, 30 or 32 wherein the medicament is administered separately or simultaneously with one or more further medicaments comprising one or several compound(s) chosen among the following groups of compounds: hematopoietic growth factors, cytokines, chemokines, monoclonal antibodies.

35. Use according to claims 33 or 34 wherein the cytokines group comprises IL-1, IL-3, IL-6, IL-11, Insulin-like growth factor 1 (IGF-1), G-CSF, GM-CSF or SCF ; the chemokines group comprises MIP-1 $\alpha$  or thrombopoietin (TPO) ; the monoclonal antibodies group comprises anti-VLA-4 antibodies.

36. Use according to any one of claims 29 to 32 wherein the further compound or medicament comprises G-CSF.

37. Use according to any one of claims 29 to 32 wherein the administration of said medicament is made by parenteral, subcutaneous, intravenous, intramuscular, intraperitoneal, transdermal or buccal routes.

38. Use according to any one of claims 29 to 32 wherein the administration of said medicament is daily or three times a day.

39. Use according to claim 31 wherein the administration of medicament comprising growth hormone

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41. Use according to any one of claims 29 to 32 wherein the administration of said medicament begins around 7 days after the beginning of a chemotherapeutic treatment or around 2 days after the end of a chemotherapeutic treatment.

42. Use of growth hormone or one of its derivatives or any factor inducing growth hormone release to prepare a medicament for preventing and/or treating opportunistic infections after transplantation or for limiting the risk of tumor recurrence after transplantation.

43. Use according to any one of claims 29 to 32 wherein growth hormone is recombinant growth hormone.

44. Use according to any one of claims 29 to 32 wherein growth hormone is human growth hormone.

45. Use according to any one of claims 29 to 32 wherein the circulating cells capable of regenerating hematopoiesis in vivo are CD34<sup>+</sup> cells.

46. Use according to claim 45 wherein the increased number of CD34<sup>+</sup> cells is more than 10, 25, 34 or 80 CD34<sup>+</sup> cells per microliter of peripheral blood after administration of the medicament.

47. Use according to claim 45 wherein the increased number of CD34<sup>+</sup> cells is at least 2x10<sup>6</sup>, 4x10<sup>6</sup>, 5x10<sup>6</sup>, 6x10<sup>6</sup>, 8x10<sup>6</sup>, 15x10<sup>6</sup> CD34<sup>+</sup> cells per kilogram of body weight after administration of the medicament.

48. Use according to any one of claims 29 to 32 wherein the increased number of circulating cells capable of regenerating hematopoiesis in vivo corresponds to around or more than 500 CFU-GM per milliliter of peripheral blood after administration of the medicament.

49. Use according to any one of claims 29 to 32 wherein the increased number of circulating cells capable of regenerating hematopoiesis in vivo corresponds to an increased level of CFU-C, CFU-Meg or BFU-E in peripheral blood after administration of the medicament.

50. Use according to any one of claims 29 to 32 wherein the increased number of circulating cells capable of regenerating hematopoiesis in vivo substantially corresponds to a white blood cell count of around or more than 1000 cells per microliter of peripheral blood after administration of the medicament.

51. Use according to any one of claims 29 to 32 wherein the increased number of circulating cells capable of regenerating hematopoiesis in vivo corresponds to around or more than  $1 \times 10^5$  GM-CFC per kilogram of body weight.

52. Use according to any one of claims 29 to 32 wherein the circulating cells capable of regenerating hematopoiesis in vivo are CD34<sup>+</sup>/CD33<sup>+</sup> cells and/or CD34<sup>+</sup>/CD38<sup>+</sup> cells and/or CD34<sup>+</sup>/Thy-I cells and/or CD34<sup>+</sup>/Thy-I/CD38<sup>+</sup> cells and/or CD33<sup>+</sup> cells and/or bone-marrow stem cells and/or progenitor cells and/or long-term culture initiating cells (LTC-IC) and/or cells that fulfill self renewal potential and/or cells that fulfill pluripotential characteristics and/or cells that initiate long term bone marrow culture and/or cells that can generate multiple cell lineages.

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53. Use according to any one of claims 29 to 32 wherein the target number of circulating cells capable of regenerating hematopoiesis in vivo is at least  $2 \times 10^4$  LTC-IC per kg of donor or recipient body, around or more than  $2 \times 10^6$  CD34<sup>+</sup> cells per kilogram of donor or recipient body weight, around or more than  $4 \times 10^6$  CD34<sup>+</sup> cells per kilogram of donor or recipient body weight or around or more than  $8 \times 10^6$  CD34<sup>+</sup> cells per kilogram of body weight.

54. Use according to any one of claims 29 to 32 wherein growth-hormone or one of its derivatives or any factor inducing growth hormone release is administered in an amount comprised between 20 to 50  $\mu\text{g/kg}$  of body weight, in an amount comprised between 30 to 40  $\mu\text{g/kg}$  of body weight or in an amount of 33  $\mu\text{g}$  per kilogram of body weight.

55. Use according to claim 36 wherein the G-CSF is administered in an amount comprised between 3 to 15 µg/kg of body weight, in an amount comprised between 4 to 12 µg/kg of body weight or in an amount of around 5 or 10 µg per kilogram of body weight.